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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,784	08/18/2003	Ulrich Feige	A-527E	8073

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,784	FEIGE ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/31/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29,40,46-51 and 63-79* is/are pending in the application.

4a) Of the above claim(s) *72-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29,40,46,47,49-51 and 63-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III (claims 26-40 and 43-51) in the reply filed on 3/31/2006 is acknowledged. The traversal is on the ground(s) that no undue burden is imposed by searching all of the claims. All of he claims concern a process directed toward the same drug Target (AGP-3) and the same molecular structure as set forth in claim 46.

In view of applicants' cancellation of the non-elected claims, applicants' arguments are moot.

Applicants election of the following species: a is 1; b is 0; X1 is -(L1)c-P1-(l2)d-P2; C is 1; D is 0; L1 and L2 is (Gly)5; P1 and P2 is a peptide sequence that modulates the activity of AGP-3 and phage display is also noted. Applicants traverse the species restriction for the same reasons stated above.

In response, to search for the different species would be undue burden since the generic compound formula contains numerous distinct species. Also, the different methods of making by the recited different processes, which materially differ from one another would be undue examination.

Status of Claims

Claims 28-29, 40, 46-51 and 63-79 are pending in the application.

Claims 72-79 and the species not encompassed by those recited above are withdrawn from consideration as being drawn to non-elected invention.

Claims 1-27, 30-39, 41-45, 48 and 52-62 have been cancelled. It is noted that the REMAKRS at page 5 made on 3/31/2006 state that claims 33-39 have been cancelled. However, the cancelled claims are claims 30-39 (not 33-39).

Claims 28-29, 40, 46-47, 49-51 and 63-71 are under examination.

Specification

The abstract of the disclosure is objected to because it is too long. Also, because of the used of the phraseology often used in patent claims e.g., "comprising". Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of **50 to 150 words**. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such

as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The disclosure is objected to because of the following informalities:

1. The status of the applications recited at page 1 has not been provided.

2. The attempt to incorporate subject matter into this application by reference to e.g., Sparks et al. (1996), Proc. Natl. Acad. Sci. 93: 1540-4, is improper because it is a publication.

The incorporation of essential material in the specification (paragraph bridging pages 30-31) by reference to the numerous World Patents e.g., WO 95/14714 and 97/08203 and publications is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing

application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors (grammatical, typographical and idiomatic). Applicants' cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-29, 40, 46-51 and 63-71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim recites for a method for preparing a pharmacologically active compound comprising the two method steps a). selecting from a library at least one peptide sequence that modulates the activity of a AGP-3 and b) preparing a compound of the recited formula wherein the peptides is 2-40 amino acids.

The disclosure at the time of filing does not describe the huge scope of the claimed components in the method. The disclosure provides only definitions for the terms used in the method. The term peptide is defined as used in the method as a 2-40 amino acids using the selection process by phage display method. Pharmacologically active is defined as a substance so described is determined to have activity that affects a medical parameter. Except for the general statements, the detailed description in the examples describe peptide library with defined structure by phage method. It describes different antagonist or inhibitor fused to Fc. It is not apparent from the examples the correlation to the huge scope of at least one peptide sequence with no definite structure except described by its function as modulators. The specification does not contain a precise definition, as by structure, formula [or] chemical name of the huge scope of the claimed at least one peptide of 2-40 amino acid residues. Adequate disclosure, like enablement,

requires representative examples, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See In re Riat (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr. (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and University of California v. Eli Lilly and Co. cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by (representative examples) for both enablement and adequate disclosure. Russell et al, (Introduction to phage biology and phage display, specifically at page 21) discloses "an assumption made when a diversified library is created for phage display is that all clones will display with similar efficiency. In fact some sequences will be refractory to display and therefore under represented in the displayed library-in the extreme. The optimal clone (e.g., the one with highest affinity) may never be isolated because it fails to display." To provide adequate written description for any type of peptide from any phage display library the specification must provide sufficient distinguishing, identifying characteristics of the genus peptide. A "written description of an invention involving a chemical genus, like a description of a chemical species,

requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). See also University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

Claims 28-29, 40, 46-51 and 63-71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include:

(1) the breadth of the claims,
(2) the nature of the invention,
(3) the state of the prior art,
(4) the level of one of ordinary skill;
(5) the level of predictability in the art,
(6) the amount of direction provided by the inventor,
(7) the existence of working examples, and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, (U.S.P.Q. 2d 1400 (CAFC 1988).

1). The specification fails to give adequate direction and guidance in how to readily go about determining which at least one peptide modulates a protein of interest to produce a functional pharmacologically active compound. It does not describe the kind, type, location and length of peptide in peptide display library that is a modulator of a protein interest. Neither does it describes the protein that has been modulated or the type of modulating effect imparted to a protein.

2). The specification failed to provide working examples for any of the numerous and different type of techniques that can be used in the instant method.

3). The breadth of the claims encompasses a large diversity of phage display library with no defined peptide structure, the predetermination of the sites of variations in a phage vector to produce the pharmacologically active peptide. It is well known in the art, that it is often difficult to know where insertions in the protein for mutations can be done without deleteriously affecting the protein function or its global structure or that of the phage organism. The diversity of the inserts is not easily estimated. It may be for example, that only a small subset of possible peptide sequences are presented

efficiently by a particular expression system. And, it is not always easy to follow the expression of peptides in particular cells; for example, to know whether or not a specific cell is expressing a member of the insert, especially for biological methods. See the Russell reference cited above.

4). The state of the prior art is such that techniques are specifically applied for a predetermined protein, phage display library.

5). The art is inherently unpredictable. See the Russell reference cited above.

6). Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art that the numerous undefined random peptide in a protein would result in a mutations having a pharmacologic activity without undue experimentation. Applicants do not adequately enable persons skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28-29, 40, 46-47, 49-51 and 63-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The steps (a) and (b) in claim 46 does not seem to correlate. Step a recites for selecting from a library. Step (b) recites for preparing a compound of the recited formula. It is not clear whether the peptide of step (a) is the compound from which the peptide is selected. Furthermore, Step (b) defines the P variables as the selected peptide sequences. Are these peptides the ones selected from step (a)? Step (a) recites only peptides without the Fc compounds of the formula. There is no identifying characteristics or features as to the kind of amino acids comprise in a dipeptide to 40 amino acids in the peptide. The process steps appear incomplete and omit essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26-32, 34, 43-46 and 48-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26-32, 34, 43-46 and 48-51 of copending Application No. ***10/653,048*** ('048 application) or 26-32, 34, 43-46 and 48-51 of copending Application No. ***10/651,723*** ('723 application) or 26-32, 34, 43-46 and 48-51 of copending Application No. ***09/563,286*** (***'***286 application***)*** or 26-32, 34, 43-46 and 48-51 of copending Application No.***10/645,***761 ('761 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the claims of the copending '048, '723, '286 and '761 recites the same broad process steps except employing different compounds distinguished

one from the other by their functions. However, the functions of the peptides do not differentiate one compound from the other. Furthermore, each of the copending applications also recite the same Fc containing compounds. The same process steps are used for each of the Fc-containing compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 26-32, 34, 43-46 and 48-51 are rejected on the ground of nonstatutory double patenting over U. S. Patent No. 6,919,426('426) or U. S. Patent No. 6,660,843 ('843) since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: the instant method is fully disclosed at col.7, line 17 up to col. 8,line 28 of ht '426 patent. See the abstract of the '843 Patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which

matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26-32, 34, 43-46 and 48-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chamow et al (TIBTECH) in view of Staten et al (WO 97/12978) or applicants' disclosure of known prior art, alone. [The rejection is based on the broad peptide attached to Fc produced by phage display library.]

Chamow et al disclose at page 56, col. 1 (referring to de Sauvage) a technique of generating a fusion protein where the Fc regions of Ig is combined with a ligand c-MPl to that recognizes a thrombopoietin receptor expressed in host cells. Table 1 at page 52 discloses the different immunoadhesin, inter alia, thrombopoietin. Fig. 3 at peg 55 shows the multimeric form of immunoadhesins. Chamow discloses at page 55 up to page 55 to

page 57 that immunoadhesins can be used as antagonists or a agonists that block or mimic physiological molecular interactions. Immunoadhesins as disclosed by Chamow at page 567 is useful in studies designed to investigate the biological functions of new or novel receptors or ligands. Phage display expression libraries are suggested at page 50. Chamow does not disclose the use of the linker, (gly)5. However, Staten et al disclose at page 33 linkers that may be composed of original peptide sequences that can be lengthened to be flexible and hydrophilic, example, (Gly)3Ser. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made prepare a compound using phage display since Chamow teaches said method or at least suggest said method. To include a linker in the fusion protein of Chamow would have been obvious (at times are optional) as linkers provide flexibility, especially those containing gly residues as taught by Staten.

Applicants at page 12, lines 9-15 states that "The compounds of this invention may be prepared by standard synthetic methods, recombinant DNA techniques, or any other methods of preparing peptides and fusion proteins….." Applicants continue at page 76, line 1 up to page 77, line 10 that "….the compounds of this invention largely may be made in transformed host cells using recombinant DNA techniques. To do

so, a recombinant DNA molecule coding for the peptide is prepared. Methods of preparing such DNA molecules are well known in the art. For instance, sequences coding for the peptides could be excised from DNA using suitable restriction enzymes. Thus at the time of applicants' invention, phage display method is well-known method of making specific peptides.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
April 15, 2006